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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,452	09/12/2006	Yingfu Li	77101-004US1	2999

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EXAMINER	
LIU, SUE XU	
ART UNIT	**PAPER NUMBER**
1639	

NOTIFICATION DATE	DELIVERY MODE
06/23/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

INFO@ORTPATENT.COM

Office Action Summary	Application No.	Applicant(s)	
	10/551,452	LI ET AL.	
	Examiner	Art Unit	
	SUE LIU	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *1-8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 September 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/27/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

1. Claims 1-20 are currently pending.

Claims 1-8 have been withdrawn.

Claims 9-20 are being examined in this application.

Election/Restrictions

2. Applicant's election of Group 3 (claims 9-20) in the reply filed on 4/20/09 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. Claims 1-8 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 4/20/09.

4. Applicant's election without traverse of the following species:

A.) with a first and second primer binding domain;

B.) with a first and second primer;

C.) with avidin coated agarose beads;

in the reply filed on /4/20/09 is acknowledged.

Priority

5. This application is filed under 35 U.S.C 371 of PCT/CA04/00482 (filed on 03/31/2004), which claims priority to US provisional application 60/458,409 (filed on 3/31/2003).

6. The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60/458,409, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application.

The '409 application does not appear to provide support for the instant claimed sequences including the sequences of SEQ ID Nos:1-5 as recited in the instant claim 15.

Thus, the instant claim 15 does not obtain the priority date of the '409 application. The effective filing date for the instant claim 15 is 3/31/2004.

Information Disclosure Statement

7. The IDS filed on 12/27/2005 has been considered. See the attached PTO 1449 form.

Specification

Sequence Rule Compliance

8. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR §§ 1.821 through 1.825 for the reason(s) below:

The instant disclosure recites lists of sequences in the drawings (e.g. Figures 1, 5, 6, etc.), which are not identified by their corresponding SEQ ID Nos in the "BRIEF DESCRIPTION OF THE FIGURES AND TABLES" of the instant specification. Applicants are requested to amend the instant specification and claims accordingly.

9. Applicants are also invited to update the continuing data (benefits claimed under 35 USC 119, 120, etc.) in the first line of the specification.

10. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification. MPEP 608.01.

Claim Rejections - 35 USC § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description Rejection

12. Claims 9-14 and 16-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims recite "An aptamer selection system comprising an antisense oligonucleotide and a library oligonucleotide, said library oligonucleotide comprising an antisense binding domain having a sequence complementary to the antisense oligonucleotide and at least one random nucleotide domain, wherein said antisense oligonucleotide is adapted to be attached to a solid support."

To satisfy the written description requirement, applicants may convey reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention.

Applicants may show possession of an invention by disclosure of drawings or structural chemical formulas that are sufficiently detailed to show that applicant was in possession of the claimed invention as a whole. See, e.g., Vas-Cath, 935 F.2d at 1565, 19 USPQ2d at 1118.

The written description requirement of 35 U.SC. 112 exists independently of enablement requirement, and the requirement applies whether or not the case involves questions of priority. The requirement applies to all inventions and includes chemical inventions. The fact that the patent is directed to method entailing use of compounds, rather than to compounds per se, does not remove patentee's obligation to provide a description of the compound sufficient to distinguish infringing methods from non-infringing methods. See Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 920-23, 69 USPQ 2d 1886, 1890-93 (Fed. Cir. 2004).

With regard to the description requirement, applicants' attention is invited to consider the decision of the Court of Appeals for the Federal Circuit, which holds that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it form other materials." University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1405 (1997), quoting Fiers v. Revel, 25 USPQ2d 1601, 1606

(Fed. Cir. 1993) (bracketed material in original) [The claims at issue in University of California v. Eli Lilly defined the invention by function of the claimed DNA (encoding insulin)].

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species or by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See Eli Lilly, 119 F. 3d at 1568, 43 USPQ2d at 1406.

Claim 9 is broadly drawn to a genus of nucleic acids with various sequences. Neither the instant specification nor the claims have demonstrated common structure and/or function for the claimed genus of nucleic acids. In addition, no representative numbers of species for each claimed genus is provided to show possession of the claimed genus of nucleic acids.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. (see MPEP 2163 II).

In this case, the instant application only provides a limited list of nucleic acid sequences with various sequences. The instant disclosure does not that there is a common core structure shared by the various disclosed nucleic acid sequences.

The Court of Appeals for the Federal Circuit, our reviewing court, has addressed the issue of what constitutes adequate written description for a claim drawn to a nucleic acid. In Enzo Biochem, Inc. v. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1602 (Fed. Cir. 2002), the court adopted a portion of the Guidelines proffered by the United States Patent and Trademark Office (USPTO). The court stated that:

> The written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of characteristics.
> Enzo Biochem, 296 F.3d at 1324, 63 USPQ2d at 1613 (citations omitted).

The court also addressed the issue of what constitutes adequate written description of a claim to a broad genus of sequences. In The Regents of The University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1998), the court determined that the disclosure of rat cDNA did not provide adequate written description support for claims drawn to mammalian and vertebrate DNA. Eli Lilly, 119 F.3d at 1567-68, 43 USPQ2d at 1405. The court stated:

> In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.
> Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.

In Enzo-Biochem, the court refined the approach advanced by Eli Lilly, adopting an example offered in the USPTO guidelines having facts that contrasted with those of Eli Lilly, wherein the written description requirement would be met. Thus, adequate written description may be present for a genus of nucleic acids based on their hybridization properties, "if they hybridize under highly stringent conditions to known sequences because such conditions dictate that all species within the genus will be structurally similar." Enzo Biochem, 296 F.3d at 1327, 63 USPQ2d at 1615.

Here, the instant claimed "oligonucletoide" having "a sequence complementary" can be any sequence that is "complementary" (including sequences that are partially complementary to other nucleic acids). For example, a nucleic acid sequence with two nucleotide residues that are complementary to a "library oligonucleotide" would be encompassed by the instant claimed oligonucleotide. Thus, the current claims encompass a myriad of nucleic acids that are not "structurally similar." This would include virtually an infinite number of possibilities. In contrast, Applicants' specification only discloses a limited number of "antisense oligos" and their corresponding complementary oligonucleotides with "random nucleotide domain".

Therefore, applicants are not in possession of the claimed genus of nucleic acids. Applicant's claimed scope represents only an invitation to experiment regarding possible antisense oligonucleotides and library oligonucleotides having complementary sequences.

Second paragraph of 35 U.S.C. 112

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 9-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9 recites "a library oligonucleotide" comprising "at least one random nucleotide domain", which the claim language is unclear. The instant claim 9 seems to recite the claimed "system" comprise "**A**" library oligonucleotide (as oppose to a library of oligonucleotides (i.e. a

plurality of oligonucleotides)). However, the instant claim 9 also recites the one "library oligonucleotide) comprising "random nucleotide domain", which implies that the one single oligonucleotide can have multiple different sequences. The instant claim 15 also seems to recites "a library oligonucleotide" (i.e. one single oligonucleotide) comprising a sequence of SEQ ID NO.2, which SEQ ID NO.2 seems to encompass multiple sequences (with the "n" residues). Thus, it is not clear if the instant claimed system comprise one single "library oligonucleotide" or multiple oligonucleotides that constitute a library (i.e. multiple oligonucleotides with different sequences.)

Claim 15 recites "a library oligonucleotid&commat" in line 2 of the said claim, which the said recitation is unclear. Appropriate correction is requested.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Sooter

16. Claims **9**, **10**, **13** and **18** are rejected under **35 U.S.C. 102(b)** as being anticipated by **Sooter** et al **(**Biol. Chem. Vol.382: 1327-1334; 2001; cited in IDS).

The instant claims recite "An aptamer selection system comprising an antisense oligonucleotide and a library oligonucleotide, said library oligonucleotide comprising an

antisense binding domain having a sequence complementary to the antisense oligonucleotide and at least one random nucleotide domain, wherein said antisense oligonucleotide is adapted to be attached to a solid support."

Claim interpretation: The underlined region of the instant claim 9 is construed as intended use of the instant claimed "antisense oligonucleotide." The intended use recitation is not afforded any patentable weight because the recitation does not appear to provide additional structural limitations.

Sooter et al, throughout the publication, teach using various nucleic acids molecules and/or library of nucleic acids. (e.g. Abstract). The reference teaches a pool of nucleic acids having various sequences (e.g. Figures 1 and 3; pp.1328+), which the pool of nucleic acids read on the library of oligonucleotide comprising a random region as recited in **clm 9**. The reference also teaches another "substrate" oligonucleotide having complementary sequence to regions of the pool of DNA (e.g. Figure 3), which the "substrate oligo" reads on the "antisense oligonucleotide" of **clm 9** as the term is broadly used in the instant disclosure. The reference also teaches the substrate oligo has an affinity tag (e.g. p.1329), which read on the intended use language.

The reference also teaches sequences at both the 5' and 3' ends (e.g. Figures 1 and 3), which the 5' and 3' end regions would read on the "primer binding domains" of the **clm 10** as the primer binding region can be any nucleic acid sequences.

The reference teaches the substrate (or the antisense oligo) was biotinylated (e.g. p.1329, left col.), which reads on **clms 13** and **18**.

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Sooter and Davis

19. Claims **9-13** and **16-20** are rejected under 35 U.S.C. 103(a) as being unpatentable over **Sooter** et al **(**Biol. Chem. Vol.382: 1327-1334; 2001; cited in IDS), in view of **Davis** et al. (PNAS. Vol.99: 11616-11621; cited in IDS).

Sooter et al, throughout the publication, teach using various nucleic acids molecules and/or library of nucleic acids, as discussed supra. The discussion under Sooter above is hereby incorporated by reference in its entirety.

Sooter et al do not explicitly teach a first and second primer as recited in **clms 11** and **19**. The reference also does not explicitly teach two random domains flanking the antisense binding domain as recited in **clms 12**, **16**, **17** and **20**.

However, **Davis** et al., throughout the publication, teach various nucleic acids (such as a library of nucleic acids) having random nucleic acids flanking a unique sequence (e.g. Figure 1;

Abstract; etc.). The Davis reference also teaches the nucleic acids comprise two primer binding regions at both ends of the nucleic acids molecules (e.g. p.11616, col.L-R; Figure 1). The reference also teaches two primers that are complementary to the primer binding regions (e.g. p.11616, right col.). The reference also teaches the advantages of having random sequences flanking a fix sequence for a library of nucleic acids so that partially structured library can be constructed to provide more efficient screening pool (e.g. Abstract).

Therefore, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to make a "system" or a composition comprising various desired nucleic acid molecules include a first oligonucleotide (such as an antisense oligo), an additional oligonucleotide having complementary sequence to the first oligonucleotide and randomly generated sequences, and corresponding amplification primer oligomers, etc.

A person of ordinary skill in the art would have been motivated at the time of the invention to make a composition comprising oligonucleotides having a fix sequence (binds to a target sequence or a sequence of interest) as well as flanking sequences that are randomly generated (especially for screening aptamers of interests), because Davis et al. teach the advantage of having partially fixed sequences (and randomly generated sequences) so that the screening efficiency can be highly improved. In addition, because both the Sooter and Davis references teach generating and using pools of nucleic acids for the purposes screening for aptamers of interest and the Sooter reference teaches aptamer specific for another nucleic acid target, it would have been obvious to one skilled in the art to substitute one nucleic acid of interest (one binding candidate) for another to achieve the predictable result of generating a collection of oligonucleotides for the desired applications.

A person of ordinary skill in the art would have been motivated at the time of the invention to make a composition comprising primers that are specific for the desired oligonucleotide, because Sooter et al. and Davis et al. teach the need for specific primers for the amplification of the desired oligonucleotides especially in a screening assay. Thus, it would have been obvious to one of ordinary skill in the art to apply the standard technique of generating complementary primers (to both ends of the oligonucleotides) as taught by both Sooter and Davis, to improve the composition/system (for screening applications) for the predicable result of enabling standard specific nucleic acid amplification through the complementary primer set.

A person of ordinary skill in the art would have reasonable expectation of success of achieving such modifications since the cited references have demonstrated the success of generating various oligonucleotides with various sequences.

Sooter, Davis and Short

20. Claims **9-14** and **16-20** are rejected under 35 U.S.C. 103(a) as being unpatentable over **Sooter** et al **(**Biol Chem. Vol.382: 1327-1334; 2001; cited in IDS) and **Davis** et al. (PNAS. Vol.99: 11616-11621; cited in IDS) as applied to claims 9-13 and 16-20 above, and further in view of **Short** et al., (PGPUB 20020006620; 1/17/2002).

Sooter et al, throughout the publication, teach using various nucleic acids molecules and/or library of nucleic acids, as discussed supra.

Davis et al., throughout the publication, teach various nucleic acids (such as a library of nucleic acids) having random nucleic acids flanking a unique sequence as discussed supra. The

discussion under the combination of Sooter and Davis above is hereby incorporated by reference in its entirety.

The combination of Sooter and Davis does not explicitly teach "avidin coated agaorse beads" as recited in **clm 14**.

However, **Short** et al., throughout the publication, teach various methods for selecting nucleic acid molecules such as aptamers (e.g. Abstract). The reference also teaches using avidin coated agarose beads for immobilizing the nucleic acids of interest (e.g. [0206]). The Short reference also teaches the advantages of using avidin coated agarose beads so that biotinylated nucleic acids can be specific isolated (e.g. [0206]).

Therefore, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to make a "system" comprising avidin coated agarose beads.

A person of ordinary skill in the art would have been motivated at the time of the invention to make a composition comprising oligonucleotides, biotinylated oligonucleotides, and avidin coated agarose beads, because Short et al. teach the advantage or need of using avidin (the specific binding partner for biotin) coated agarose beads for efficient and specific isolation of nucleic acid molecules. In addition, because both all the cited references teach using appropriate binding pairs (such as biotin-streptavidin or biotin-avidin) for immobilizing (or isolating) nucleic acids of interests, it would have been obvious to one skilled in the art to substitute one type of coated solid support (streptavidin coated beads) for other (avidin coated beads) to achieve the predictable result of binding oligonucleotides of interests.

A person of ordinary skill in the art would have reasonable expectation of success of achieving such modifications since the cited references have demonstrated the success of generating various oligonucleotides and using various solid supports.

Sooter, Davis2 and Short

21. Claims **9-14** and **16-20** are rejected under 35 U.S.C. 103(a) as being unpatentable over **Sooter** et al **(**Biol Chem. Vol.382: 1327-1334; 2001; cited in IDS) and **Davis** et al. (WO02/06827; 1/24/2002) as applied to claims 9-13 and 16-20 above, and further in view of **Short** et al., (PGPUB 20020006620; 1/17/2002).

Sooter et al, throughout the publication, teach using various nucleic acids molecules and/or library of nucleic acids. (e.g. Abstract). The reference teaches a pool of nucleic acids having various sequences (e.g. Figures 1 and 3; pp.1328+), which the pool of nucleic acids read on the library of oligonucleotide comprising a random region as recited in **clm 9**. The reference also teaches another "substrate" oligonucleotide having complementary sequence to regions of the pool of DNA (e.g. Figure 3), which the "substrate oligo" reads on the "antisense oligonucleotide" of **clm 9** as the term is broadly used in the instant disclosure. The reference also teaches the substrate oligo has an affinity tag (e.g. p.1329), which read on the intended use language.

The reference also teaches sequences at both the 5' and 3' ends (e.g. Figures 1 and 3), which the 5' and 3' end regions would read on the "primer binding domains" of the **clm 10** as the primer binding region can be any nucleic acid sequences.

The reference teaches the substrate (or the antisense oligo) was biotinylated (e.g. p.1329, left col.), which reads on **clms 13** and **18**.

Sooter et al do not explicitly teach a first and second primer as recited in **clms 11** and **19**. The reference also does not explicitly teach two random domains flanking the antisense binding domain as recited in **clms 12**, **16**, **17** and **20**. The reference also does not explicitly teach "avidin coated agaorse beads" as recited in **clm 14**.

However, **Davis** et al., throughout the publication, teach various nucleic acids (such as a library of nucleic acids) having random nucleic acids flanking a unique sequence (e.g. Figure 1; Abstract; etc.). The Davis reference also teaches the nucleic acids comprise two primer binding regions at both ends of the nucleic acids molecules (e.g. p.26+; Figures 1-2). The reference also teaches two primers that are complementary to the primer binding regions (e.g. p.26+; p.34+; Figures 1-2). The reference also teaches the advantages of having random sequences flanking a fix sequence for a library of nucleic acids so that partially structured library can be constructed to provide more efficient screening pool (e.g. Abstract).

In addition, **Short** et al., throughout the publication, teach various methods for selecting nucleic acid molecules such as aptamers (e.g. Abstract). The reference also teaches using avidin coated agarose beads for immobilizing the nucleic acids of interest (e.g. [0206]). The Short reference also teaches the advantages of using avidin coated agarose beads so that biotinylated nucleic acids can be specific isolated (e.g. [0206]).

Therefore, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to make a "system" or a composition comprising various

desired nucleic acid molecules include a first oligonucleotide (such as an antisense oligo), an additional oligonucleotide having complementary sequence to the first oligonucleotide and randomly generated sequences, and corresponding amplification primer oligomers, etc. It would also have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to make a "system" comprising avidin coated agarose beads.

A person of ordinary skill in the art would have been motivated at the time of the invention to make a composition comprising oligonucleotides having a fix sequence (binds to a target sequence or a sequence of interest) as well as flanking sequences that are randomly generated (especially for screening aptamers of interests), because Davis et al. teach the advantage of having partially fixed sequences (and randomly generated sequences) so that the screening efficiency can be highly improved. In addition, because both the Sooter and Davis references teach generating and using pools of nucleic acids for the purposes screening for aptamers of interest and the Sooter reference teaches aptamer specific for another nucleic acid target, it would have been obvious to one skilled in the art to substitute one nucleic acid of interest (one binding candidate) for another to achieve the predictable result of generating a collection of oligonucleotides for the desired applications.

A person of ordinary skill in the art would have been motivated at the time of the invention to make a composition comprising primers that are specific for the desired oligonucleotide, because Sooter et al. and Davis et al. teach the need for specific primers for the amplification of the desired oligonucleotides especially in a screening assay. Thus, it would have been obvious to one of ordinary skill in the art to apply the standard technique of generating complementary primers (to both ends of the oligonucleotides) as taught by both Sooter and

Davis, to improve the composition/system (for screening applications) for the predicable result of enabling standard specific nucleic acid amplification through the complementary primer set.

A person of ordinary skill in the art would have been motivated at the time of the invention to make a composition comprising oligonucleotides, biotinylated oligonucleotides, and avidin coated agarose beads, because Short et al. teach the advantage or need of using avidin (the specific binding partner for biotin) coated agarose beads for efficient and specific isolation of nucleic acid molecules. In addition, because both all the cited references teach using appropriate binding pairs (such as biotin-streptavidin or biotin-avidin) for immobilizing (or isolating) nucleic acids of interests, it would have been obvious to one skilled in the art to substitute one type of coated solid support (streptavidin coated beads) for other (avidin coated beads) to achieve the predictable result of binding oligonucleotides of interests.

A person of ordinary skill in the art would have reasonable expectation of success of achieving such modifications since the cited references have demonstrated the success of generating various oligonucleotides and using various solid supports.

Conclusion

SEQ ID No. 1 is free of prior art searched.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached at 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Sue Liu/
Primary Examiner, AU 1639
6/11/09